2. DESCRIPTION OF THE PROPOSED EXPERIMENT IN NON TECHNICAL LANGUAGE

Cystic fibrosis (CF) is a common inherited disease among the white population of Europe and North America. It is characterized by chronic infection and obstruction of the airways leading to the lungs. Patients usually die from the disease by their mid-to-late twenties. The recent discovery and characterization of the inherited material - the gene - that causes the disease has lead to a rapid increase in our knowledge of the basic defect responsible for the disease state, and has raised the possibility of treating CF by giving to the patient a good copy of the CF associated gene. This is a new approach to the treatment of inherited diseases, called gene therapy.

Eventually gene therapy for cystic fibrosis might be achieved by treating the airways of CF patients with a "tailor-made" virus that has been altered to make it less infectious and to include the CF gene. One possible virus to do this is called adenovirus. It is normally associated with minor respiratory infections, such as colds. Although adenoviruses have been used safely in the past as vaccines, we need to establish the feasibility and safety of using such an approach.

The authors of this proposal have already treated three CF patients with very small amounts of CF-adenovirus and shown it is possible to correct the basic defect associated with the disease. Virus was applied to a small area within the nose and a small electrode used to measure the tiny voltage that normally exists across the lining of the nose. In patients with CF, this voltage is abnormal because of a defect in the CF gene. After administration of virus, this voltage was restored to normal for the few days tested.

We now hope to extend these studies to ascertain whether it is safe to administer larger amounts of virus, whether it is safe to administer it more than once, and whether we can detect evidence of clinical improvement. To do this, virus will be applied to the nose or to the sinus. By using these organs, we can obtain the data we wish to measure without using large amounts of virus or using invasive clinical protocols. In this way, we hope to maximize patient safety, while at the same time determining whether adenovirus is likely to be safe and to be efficacious.